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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/701,674	11/28/2000	Preeti Lal	PF-0539 USN	8930

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 01/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/701,674	LAL ET AL.	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *1,2,7,8 and 15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6 and 9-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement is made of applicants election with traverse of polynucleotides, fragments, variants, expression vectors and host cells and a method of expressing the polynucleotide of a host cell. Acknowledgment is also made of applicants further election with traverse of the polynucleotides encoding SEQ ID NO:23 and the polynucleotide of SEQ ID NO:54.

The traversal of the first election is on the grounds that the claims have unity of invention. This has been considered but not found persuasive. Applicant has failed to point out the special technical feature shared by each of the polynucleotides or the polypeptides encoded therefrom. Further, the claims are not novel over the prior art as evidenced by the art rejections below. Therefore the claims lack a special technical feature which renders a special contribution over the prior art. Thus, the claims lack unity of invention because of the lack of a special technical feature which is novel in the art.

The traversal of the second election is based on section 803.04 of the MPEP which states that "up to ten independent an distinct nucleotide sequence will be examined in a single application without restriction". This has been considered but not found persuasive. Firstly, "up to 10" includes one sequence. Secondly, the PTO does not have the computer resources to commit to searching electronic databases for ten polynucleotide sequences per application. In order to best share the PTO resources over all pending applications it is necessary to restrict the number of polynucleotide sequences searches in each application. Thus, the searching of all the polynucleotide sequence in the instant application would result in an undue burden of search. The restriction requirement is deemed proper and adhered to.

Claims 1-20 are pending. Claims 1, 2, 7, 8 and 15-20, drawn to non-elected inventions, are withdrawn from consideration. Claims 3-6 and 9-14 are examined on the merits.

Priority

Acknowledgment is made of a claim to an earlier effective filing date via the provisional applications 60/089,029, 60/094,575 and 60/104,624. Upon review of each of these applications it is noted that only the '575 application discloses the instant SEQ ID NO:54 encoding SEQ ID NO:23, therefore the effective priority date for the instant claims will be July 29, 1998.

Claim Objections

Claim 3 is objected to for being dependent on a non-elected invention. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 and 9-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is vague and indefinite in the recitation of "stringent conditions". All hybridization conditions have some degree of stringency, low, moderate or high, Therefore the physical parameters which determine the specific polynucleotides which hybridize are unclear. Therefore the metes and bounds of polynucleotide which fulfill the specific embodiments of the claims are unclear.

It is unclear if claim 9 encompasses polynucleotide fragments of SEQ ID NO:54 or polynucleotides comprising fragments of SEQ ID NO:54. For purpose of examination, both alternatives will be considered.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for host cells which are made in vitro, does not reasonably provide enablement for host cells which are made in vivo. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

The specification states that a vector capable of expressing PRGE may be administered to a subject to treat or prevent a disorder characterized by decreased expression or activity or PRGE (page 28, lines 5-7). This introduction of vectors into subjects in need thereof is in the realm of gene therapy and is not enabled by the specification for the following reasons.

The instant specification does not teach how to overcome problems with in vivo delivery and expression with respect to the administration of the claimed nucleic acids or viral vectors comprising said nucleic acids. The state of the art as of the priority date sought for the instant application is that in vivo gene delivery is not well developed and is highly unpredictable. For instance Verma et al (Nature, 1997, Vol. 389, pp. 239-242) teach that the Achilles heel of gene therapy is gene delivery. Verma et al state that the ongoing problem is the inability to deliver genes efficiently and to obtain sustained expression (page 239, column 3). Eck et al (Gene-Based Therapy, In: The Pharmacological Basis of Therapeutics, Goodman and Gilman, Ed.s, 1996, pp. 77-101) teach that the fate of the DNA vector itself with regard to the volume of distribution, rate of clearance into tissues etc., the in vivo consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA the level of mRNA produced, the stability of the mRNA produced in vivo, the amount and stability of the protein produced and the proteins compartmentalization or secretory fate within the cell are primary considerations regarding effective therapy. Eck et al state that these factors differ dramatically on the vector used, the protein being produced, and the disease being treated (Eck et al bridging pages 81-82).

As of the priority date sought, it was well known in the art how to infect or transfect cells in vitro or ex vivo with viral vectors. However, using viral vectors to deliver DNA to an organism in vivo, or using infected or transfected cells to deliver nucleic acids which encode a particular protein sequence to an organism in vivo is in the realm of gene therapy, and as of the priority date sought, highly unpredictable in view of the complexity of in vivo systems. Orkin et al state ("Report and Recommendation of the Panel to Assess the NIH Investment in Research on Gene Therapy", NIH, 1995) clinical efficacy had not been definitively demonstrated with any

gene therapy protocol (page 1, second paragraph). Orkin et al defines gene therapy as the transfer of DNA into recipient cells either ex vivo or in vivo (page 7, under the heading "Gene transfer"), thus encompassing the instant claims drawn to the administration of antigen presenting cells transfected or infected ex vivo. Orkin et al concludes that, "none of the available vector systems is entirely satisfactory, and many f the perceived advantages of vector systems have not been experimentally validated. Until progress is made in thee areas, slow and erratic success in applying gene transfer methods to patients can be expected" Orkin et al comment that direct administration of DNA or DNA in liposomes is not well developed and hindered by the low efficiency of gene transfer (page 8, paragraph 5). Orkin et al teach that adequate expression of the transferred genes is essential for therapy, but that data regarding the level and consistency of expression of transferred genes in animal models was unknown. Orkin et al states that in protocols not involving ex vivo infections/transfection, it is necessary to target the expression of the transferred genes to the appropriate tissue or cell type by means of regulatory sequences in gene transfer vectors. The specification does not teach a vector having a specific regulatory sequence which would direct the expression of the nucleic acids within the appropriate tissue type. The specification does not remedy any of the deficiencies or the prior art with regard to gene therapy. Given the lack of any guidance from the specification on any of the above issues pointed out by Verma or Eck or Orkin. One of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to make the claimed host cell in vivo.

Amendment of the claim to recited "isolated" host cell would overcome this rejection.

Claims 3-6 and 9-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

Claim 3 is drawn in part to an isolated and purified polynucleotide encoding the fragments of SEQ ID NO:23. Claim 4 is drawn to an isolated polynucleotide variant having at least 90% sequence identity to polynucleotide encoding the polypeptide comprising SEQ ID

NO:23 and fragments thereof. Claim 5 is drawn to an isolated polynucleotide which hybridizes under stringent conditions to the polynucleotide of claim 3. Claim 6 is drawn to a polynucleotide which is complementary to the polynucleotide of claim 3. Claim 9 is drawn in part to a polynucleotide comprising fragments of SEQ ID NO:54, Claim 10 is drawn to a polynucleotide variant having at least 90% sequence identity to the polynucleotide of claim 9. Claim 11 is drawn to a polynucleotide which is complementary to the polynucleotide of claim 9. Claim 12 is drawn to an expression vector comprising at least a fragment of the polynucleotide of claim 3. Claim 13 is drawn to a host cell comprising the expression vector of claim 12. Claim 14 is drawn to a method for producing a polypeptide comprising culturing the host cell of claim 13 and recovering the polypeptide from the host cell culture

The instant claims are drawn to polynucleotides encoding fragments of SEQ ID NO:23, polynucleotides comprising fragments of SEQ ID NO:54. The instant claims are also drawn to variant nucleic acids having at least 90% sequence identity to SEQ ID NO:54, or 90% sequence identity to a fragment of SEQ ID NO:54 or 90% identity to a polynucleotide encoding SEQ ID NO:23 or 90% sequence identity to a polynucleotide encoding a fragment of SEQ ID NO:23. The claims are thus drawn to a genus of variant polypeptides encompassing sequence variants and fragments and polynucleotides which minimal comprise fragments of SEQ ID NO:54 or fragments encoding SEQ ID NO:23. The claims are not limited by the function of the polynucleotides or the function of a polypeptide encoded thereby. Thus the genus of polynucleotides claimed is highly variant encompassing polynucleotides which differ widely in structure and function from SEQ ID NO:54 and the polynucleotides encoding SEQ ID NO:23. The specification describes only SEQ ID NO:54 and the polynucleotides encoding SEQ ID NO:54. This description fails to describe the entirety of the genus claimed because the genus encompasses
many members which differ in both structure and function from that of the polynucleotide encoding SEQ ID NO:23 and SEQ ID NO:54. One of skill in the art would reasonable conclude that applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 3-6 and 9-13 are rejected under 35 U.S.C. 102(a) as being anticipated by Quaggin et al (Mechanisms of Development, 1998, Vol. 71, pp. 37-48). Quaggin et al disclose the cDNA encoding POD-1 which is 98.% identical to SEQ ID NO:54, comprises a fragment of SEQ ID NO:54 from nucleotide 8 to nucleotide 448 and from nucleotide 450 to nucleotide 1261. The encoded POD-1 is 99.6% identical to the instant SEQ ID NO:23. Quaggin et al disclose vectors and host cells comprising cDNA encoding POD-1 (page 38, section 2.1).

Claims 3-6 and 9-14 are rejected under 35 U.S.C. 102(a) as being anticipated by Hidai et al (Mechanisms of Development, 1998, Vol. 73, pp. 33-43).

Hidai et al disclose capsulin encoded by a polynucleotide comprising nucleotides 42-161of the polynucleotides encoding SEQ ID NO:23. Hidai et al disclose vectors, host cells and a method of expressing capsulin (page 38, section 2.4 and page 42, section 4.4). The disclosure of Hidai et al fulfills the specific embodiments of a fragment of the polypeptides encoding SEQ ID NO:23 as well because a fragment can read on a single nucleotide.

Claims 4-6 and 10 are rejected under 102(e) as being anticipated by Au-Young et al (US 6,500,938).

Au-Young et al disclose Sequence Identifier 1028 which is 97.9% identical to a fragment of a polynucleotide encoding SEQ ID NO:23 and 97.9% identical to a fragment of SEQ ID NO:54 as evidenced by the attached sequence alignment. Au-Young et al disclose the complement of SEQ ID NO:1028 (claim 2) which fulfills the specific embodiment of claim 6. It is noted that the instant specification defines complementarity as encompassing partial complements (page 10, lines 12-14). The complementary sequence would hybridize under conditions of low stringency to the instant polynucleotides encoding SEQ ID NO:23.

Claims 5, 6, 9, 10, 11 are rejected under 35 U.S.C. 102(b) as being anticipated by the New England Biolabs Catalog (1993-1994, page 91) which discloses random primers which hybridize under conditions of lowered stringency to the instant polynucleotides and which are complementary to the instant polynucleotides and which are fragments of SEQ ID NO:54 and which would hybridize to the polynucleotides encoding SEQ ID NO:23.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

An obviousness-type double-patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. In reBerg, 140 F.3d, 1428, 46 USPQ2d 1226 (Fed. Cir. 1998): In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993): In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 4-6 and 10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,500,938. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-5 of the '938 patent anticipate the instant claims to the extent that they read on SEQ ID NO:1028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571)272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella

KAREN A. CANELLA PH.D
PRIMARY EXAMINER

Karen A Canella, Ph.D.
12/27/2004